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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/783,083	02/15/2001	Avinoam Dukler	00/21362	3267

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EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/783,083

Applicant(s)

DUKLER ET AL.

Examiner

Jon D Epperson

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 September 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 65-74 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 65-74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9/30/2003 6) ☐ Other:

## **DETAILED ACTION**

### ***Request for Continued Examination (RCE)***

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/29/03 has been entered. Claims 1-64 have been canceled and new claims 65-74 have been entered. Therefore, claims 65-74 are pending and active in the instant application. An action on the merit follows.

2. Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

### **Withdrawn Objections/Rejections**

3. The rejections under 35 U.S.C. § 112, second paragraph, drawn to the omitted essential steps (see Paper No. 12, paragraph 16) is withdrawn in view of Applicants' amendments and/or arguments. The rejections under 35 U.S.C. § 112, first paragraph (New Matter) are hereby withdrawn in view of Applicants' amendments and/or arguments. The Fodor et al and Dower et al rejections under 35 U.S.C. 103(a) are withdrawn in view of Applicants' amendments and/or arguments. All other rejections are maintained and the arguments are addressed below.

**Outstanding Objections and/or Rejections**

***Claim Rejections - 35 USC § 112 – Maintained Rejection***

4. Claims 65-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the limited number of complex carbohydrate libraries disclosed, does not reasonably provide enablement for *any* complex carbohydrate library especially complex carbohydrates that contain “non-natural” carbohydrates, which claim 65 literally encompasses as a result of Applicants’ “comprising” terminology. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The scope of claim 65 encompasses complex carbohydrate libraries with carbohydrate members that are unbounded by the number of saccharide subunits, substituents or the degree and type of linkages between saccharide units or saccharide units and other substituents because the “comprising” terminology still allows for complex carbohydrates of all sizes and shapes. Furthermore, claim 65 encompasses complex carbohydrate libraries, which contain carbohydrate members that have yet to be prepared or envisioned. Furthermore, claim 65 encompasses complex carbohydrate libraries, which contain unusual or unnatural sugars as substrates, which may not be good substrates for the enzymes disclosed by applicant. Consequently, the examples set forth in the specification do not constitute support for the entire scope of claims 65-74 and, as a result, the entire scope of claims 65-74 could not be supported without undue experimentation.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is “undue.” These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: Claim 65 is drawn to a method comprising the steps of “producing an addressable combinatorial complex carbohydrate library.” Such a claim represents a broad scope because it reads on all possible complex carbohydrates (even ones that have yet to be synthesized) including complex carbohydrate libraries that contain unusual or unnatural sugars as a result of the “comprising” terminology, which may not be good substrates for the enzymes disclosed by applicants.

(3 and 5) The state of the prior art and the level of predictability in the art:

According to the applicants, “[a]lthough carbohydrate libraries of limited complexity have been synthesized using various chemical methods, a combinatorial library of complex carbohydrates with a high rank of structural complexity resembling natural complex carbohydrates (e.g., highly branched structures) has not yet been produced” (see page 10 of specification, lines 11-15). The applicants further state that “the unavailability of an efficient and comprehensive synthesis method applicable for producing diverse and

complex carbohydrate species” has led to a lag in discovering new carbohydrate-derived pharmaceutical reagents (see page 14 of specification, lines 16-20). Consequently, the state of the prior art does not provide adequate guidance for one of skill in the art to predict how to synthesize *any* complex combinatorial carbohydrate library (especially those libraries not disclosed by the applicants) without undue experimentation especially libraries that contain unusual or unnatural sugars.

Furthermore, the use of enzymes in synthetic reactions are inherently “unpredictable” because unpredictable steric effects often prevent the desired enzymatic reaction. For example, applicant verified the  $\beta$ -1,4-galactosyltransferase mediated addition of  $\beta$ -D-galactose to “the plate immobilized phenyl- $\beta$ -D-GlcNAc” using a 22 atom linker, but was not able to detect any transfer of  $\beta$ -D-galactose to “the plate immobilized  $\beta$ -D-GlcNAc” using a 20 atom linker. The applicant “suggested” that the differences in reactivity were caused by the small change in “linker length” i.e., 22 to 20 atoms, which clearly demonstrates the “unpredictable” nature of these enzymatic reactions (see page 81, lines 13-19). Furthermore, applicant acknowledges this limitation and others by stating that the “linker length, flexibility of the complex carbohydrate, immobilization of carbohydrate groups and steric hinderance are also important factors effecting synthesis efficiency” (see page 87, lines 4-6).

In addition, Sears et al states “[a]nother drawback of the enzymatic approach is that while enzymes are excellent at catalyzing the synthesis of natural products, their ability to accept novel saccharides with unusual or unnatural sugars as substrates may be poor; at best, it will be unknown. Models for the substrate preferences of glycosyltransferases are

currently unavailable, and alteration of their specificity using protein engineering has experienced limited success" (see Sears, P.; Wong, C. -H. 'Strategies for Creating the Diversity of Oligosaccharides' In: Handbook of Combinatorial Chemistry Edited by K. C. Nicolaou et al. Weinheim: Wiley-VCH, 2002, Vol. 2, p. 713).

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level. Such persons of ordinary skill in this art, given its unpredictability (see above), would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have only provided a limited number of working examples describing complex carbohydrate libraries that would not adequately instruct one of ordinary skill in the art to synthesize *every* complex carbohydrate library. Furthermore, applicant has not provided any examples of complex carbohydrate libraries with unnatural sugars, which may not be good substrates for the enzymes disclosed by applicant.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The quantity of experimentation needed to make or use the claimed invention would be great. The art is inherently unpredictable (see above). The preparation of the complex carbohydrate libraries is unpredictable because there is no general glycosylation methodology for the preparation of linked saccharide units that proceeds quantitatively and stereospecifically. Furthermore, the list of enzymes provided by applicant would not provide for a means to synthesize *all* complex carbohydrates.

Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. (See *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991)). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

#### *Response to Arguments*

5. Applicant's arguments have been fully considered but they are not found persuasive. The Examiner's rationale is set forth below. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that the new claim limitations added clearly define the nature and size of the complex carbohydrate structures used and, as a result, the disclosure is enabled (see 10/29/2003 Response, page 4, last three paragraphs).

The Examiner contends that Applicants' use of "comprising" terminology still allows for complex carbohydrates of all sizes and shapes and, as a result, the Examiner does not agree that the "nature and size" of the complex carbohydrates has been clearly defined especially since non-natural complex carbohydrates would also be encompassed.



***35 USC § 112, second paragraph – Maintained Rejection***

6. Claims 65-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For claims 65-66, 68-71 and 73-74, the term “complex carbohydrate” is a relative term, which renders the claim indefinite. The term “complex carbohydrate” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, the applicants have not disclosed the number of monomers, the amount of branching, or the type of linkages that would be required for an oligomer to be classified as a “complex carbohydrate.” Furthermore, the specification does not provide a standard for ascertaining these limitations because according to Figures 2 and 3, a complex carbohydrate may contain any number of monomers and any number of branch points (there are entries in the CarbBank database showing single monomer complex carbohydrates with no branch points). Therefore, it is not possible to determine the metes and bounds of the invention as claimed. Consequently, claims 65-66, 68-71 and 73-74 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner further contends that the literature does not provide a consistent definition for the term “complex carbohydrate” and, as a result, the metes and bounds of the claimed invention cannot be determined in light of the specification, which does not

provide a clear definition for the term either (e.g., see Anderson et al, page 2, paragraph 2 which states that “[t]he term ‘complex carbohydrate’ ... is ... poorly defined and means different things for various countries and for different researchers” (see Anderson et al, page 2, paragraph 2) (emphasis added) (Anderson, H.; Lamb, M.; Mendelson, R.; Ocana, A. M.; Stephen, A. M.; O’Brien, H. T. “The Carbohydrate Controversy Persists” Carbohydrate News, Issue 1, 1995, 1-7).

B. For **claim 65, 70**, the term “naturally occurring monosaccharides” is vague and indefinite because a person of skill in the art would not be able to immediately envision all of the different monosaccharide structures that occur in nature. A person of skill in the art could only envision those compounds that have been discovered and/or isolated from nature and that have been sufficiently characterized using NMR, X-ray crystallography or other comparable physical method that would allow a person of skill in the art to ascertain their chemical structures. However, a person of skill in the art could not immediately envision those “naturally occurring” monosaccharides that have not yet been discovered and/or isolated and/or characterized. Consequently, the metes and bounds of the claimed invention cannot be determined. Therefore, claims 65, 70 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

### *Response to Arguments*

7. Applicant's arguments have been fully considered but they are not found persuasive. The Examiner's rationale is set forth below. Please note that the above rejection has been modified

from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "new independent claims 65 and 70 now recite limitations which clearly define the size of the complex carbohydrates of the library" (see 10/29/2003 Response, page 5, paragraphs 1-4).

These arguments were not found persuasive for the following reasons:

The Examiner contends that the limitations that have been added i.e., "plurality of complex carbohydrate structures is composed of at least 2 and no more than 20 naturally occurring monosaccharide units" further define the claimed invention, NOT the term "complex carbohydrate" and, as a result, the term still remains vague and indefinite for the reasons of record (i.e., Applicants do not state in their specification that the term "complex carbohydrate" is defined as a carbohydrate with 2 to 20 naturally occurring monosaccharide units). In addition, the Examiner does not agree that "new independent claims 65 and 70 now recite limitations which clearly define the size of the complex carbohydrates" because Applicants use "comprising" terminology that is open-ended and would include the addition of other chemical groups that could change the size and/or complexity of the carbohydrate.

Furthermore, the Examiner contends that Applicants have not set forth any arguments to refute the outstanding rejection drawn to "naturally occurring" monosaccharides and, as a result, the rejection is maintained.

***35 USC § 102 – Maintained Rejection***

8. Claims 65, 68-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al (U.S. Patent No. 5,424,186) (Date of Patent is **June 13, 1995**).

For ***claims 65, 68-69***, Fodor et al (see entire document) disclose a method for the directed spatially addressable “synthesis and use of diverse polymer sequences on a substrate” wherein a complex carbohydrate chip was formed (see Fodor, column 2, lines 32-33), which anticipates claims 65. For example, Fodor et al discloses the production of complex polysaccharides on an addressable VLSIPS chip using enzymatic synthesis wherein a specific example is given for complex carbohydrate structures that include at least two covalently attached identical saccharide units wherein some of the disaccharides are not naturally occurring and some of the disaccharides are naturally occurring (see Fodor et al, columns 68-69, Section V B, see especially column 69, paragraph 2). Fodor et al also discloses that the complex carbohydrates can be branched (e.g., see Fodor et al, column 16, lines 22-26, “Those of skill in the art will also note that more than one functional group can be employed on ... the monomer, i.e., to facilitate the synthesis of branched ... structures”; see also column 17, line 59; see also column 7, lines 35-48). Furthermore, Fodor et al disclose “parallel” synthesis (e.g., see column 10, line 4). Finally, the Examiner notes that “only” a single structure could be produced on a “single” chip at a “single” location i.e., the complex carbohydrate cannot “simultaneously” be two different complex carbohydrate structures at a given location on a “single” chip.

***Response***

9. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "no clear description or suggestion of synthesis of branched polysaccharides using enzymatic approaches is set forth ... Rather, Fodor et al. concentrate on outlining a chemical synthesis approach which is highly suitable for the parallel synthesis of linear polymers such as polypeptides and polynucleotides, and can also be applied to the synthesis of linear polysaccharides." (see 10/29/2003 Response, page 5, last paragraph).

[2] Applicants argue, "enzymatic synthesis ... has several advantages ... predetermined structure and stereo-specificity ... specific and uniform branching patterns" (see 10/29/2003 Response, pages 6-7) that Fodor et al presumably lack.

[3] Applicants argue, "that although Fodor et al. mentions branched synthesis on column 16 lines 22-26 this text does not, in any way, describe enzymatic synthesis of branches ... [and] cannot be utilized to generate a population of complex carbohydrates of a single branched structure" (see 10/29/2003 Response, page 7, paragraph 3).

[4] Applicants argue that Fodor et al do not provide any enablement or written description for a method of generating branched structures (see 10/29/2003 Response, page 7, paragraph 4).

[5] Applicants argue, "In addition, it should also be noted that although combining chemical synthesis with enzymatic reactions is theoretically possible, in the case of Fodor et al. such combination would not since the monosaccharides building blocks utilized by the method described by Fodor et al are modified (i.e., include a protective group) and as was noted by the Examiner with respect to this application, enzymatic reactions which target such modified saccharides would not be efficient and accurate (see 10/29/2003 Response, paragraph bridging pages 7-8).

[6] Applicants argue that the chemical linker imparts unique and favorable properties that Fodor et al do not have.

This is not found persuasive for the following reasons:

[1] In response to applicants' argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "branched" polysaccharides) are not recited in the rejected claim(s) i.e., claims 65 and 69. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For claim 68 that does recite "branched" complex carbohydrates the Examiner notes that that Fodor et al do teach branched polysaccharides (see amended rejection above, e.g., column 16, lines 22-26, "Those of skill in the art will also note that more than one functional group can be employed on ... the monomer, i.e., to facilitate the synthesis of branched ... structures"). Fodor et al further states that the "monomers" used to synthesize the "branched" structures can be "[a] member of a set of small molecules which can be joined together to form a polymer. The set of monomers includes ... the set of pentoses and hexoses [i.e., monomers used to make

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polysaccharides]”). If the “branched” structures do not refer to polypeptides, polynucleotides or polysaccharides (as Applicants contends above) then the statement in column 16, lines 22-26 would have no meaning (i.e., the monomers would not refer to anything), which would not be a reasonable interpretation of the Patent.

[2] The Examiner further contends in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., enzymatic synthesis, stereospecificity, specific and uniform branching patterns) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Dower et al teach the use of enzymes and thus also teach the advantages that Applicants outline including stereo-specific synthesis of branched complex carbohydrates (see Fodor et al, columns 68-69, Section V B, see especially column 69, paragraph 2 which outlines the use of “enzyme” synthesis; see also column 16, lines 22-26, “Those of skill in the art will also note that more than one functional group can be employed on ... the monomer, i.e., to facilitate the synthesis of branched ... structures”).

[3] In response to applicants' argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., “single branched structure”) are not recited in the rejected claim(s) i.e., claims 65 and 69. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For claim 68, the Examiner contends that “all” carbohydrates at “each” addressable location will have a “single” structure because a carbohydrate cannot “simultaneously” be two different molecules at once. Consequently, this limitation does not distinguish the claimed invention from Fodor et al because Fodor et al also contain a “single” structure at “each” addressable position (i.e., chemical synthesis might produce both  $\alpha$  and  $\beta$  anomers, but it would NOT produce both  $\alpha$  and  $\beta$  anomers at the “same” addressable location at the same time). Therefore, Applicants have not sufficiently distinguished “enzymatic” from “chemical” synthesis using this phraseology. In addition, Fodor discloses the use of enzymes that would produce single stereoisomers.

[4] The Examiner further contends, “When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980)” (see MPEP § 2121). Here, Applicants have not met their burden for rebutting the presumption of operability.

First, Fodor et al uses BOTH “enzymatic synthesis” (e.g., see column 69, paragraph 2 disclosing the use of galactosyl transferases) and “chemical synthesis” to produce the carbohydrate chips. However, Applicants’ statements with regard to enablement and written description fail to address the “enzymatic synthesis” and, as a result, do not fully rebut the operability of Fodor et al (i.e., it is Applicants’ burden to rebut the entire reference, not just selected portions). Applicants limit their discussion to the first “protected” sugar and do not



discuss the “enzymatic” addition of more monomers to the growing chain of the saccharide as was described in column 69, paragraph 2).

Second, Applicants statements that the “chemical synthesis” (e.g., use of photolabile protecting groups) would be “time consuming experimentation in order to formulate an approach which can be effectively used to generate branched carbohydrates of a predetermined structure” (e.g., see Paper No. 15, page 8, paragraph 3) are wholly unsubstantiated and are also refuted by Fodor et al and the prior art. The Examiner contends that Fodor et al do disclose at least one “approach” for producing branched structures (e.g., see Fodor et al, column 16, lines 22-26, “Those of skill in the art will also note that more than one functional group can be employed on ... the monomer, i.e., to facilitate the synthesis of branched ... structures”; see also column 17, line 59; see also column 7, lines 35-48). Here, the “approach” is simply to use “more than one functional group” on either the linker or the monomer to make the branched structure i.e., “chemical synthesis” with or without the addition of “enzymatic synthesis”. Furthermore, Fodor et al state that “[t]hose of skill in the art” will readily be able to do this, which directly refutes Applicants statements. Furthermore, the Examiner contends that the use of other enzymes to make both branched and linear carbohydrates (i.e., “enzymatic synthesis”) would be immediately envisioned by one of skill in the art because the use of these enzymes in creating branched carbohydrates was routine (see 35 U.S.C. § 103 rejection, below).

Third, the Examiner notes, “[i]n determining that quantum of prior art disclosure which is necessary to declare an applicant’s invention not novel’ or anticipated’ within section 102, the stated test is whether a reference contains an enabling disclosure’... .” *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an “enabling disclosure” if the public

was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985)" (see MPEP § 2121.01). Here, the Examiner sets forth Nicolaou et al (Nicolaou, K. C.; Watanabe, N.; Li, J.; Pastor, J.; Winssinger, N. "Solid-Phase Synthesis of Oligosaccharides: Construction of a Dodecasaccharide" *Angew Chem. Int. Ed.* 1998, 37(11), 1559-16561) (IDS Reference AB in Paper No. 16), which clearly shows that making "branched" oligosaccharides on a solid-support without the use enzymes was clearly within the knowledge of a person of ordinary skill (e.g., see Nicolaou et al, scheme 2 showing branched oligosaccharide made solely by "chemical" synthesis employing different reactive groups as stated in Fodor et al). Therefore, Fodor et al is enabled.

[5] The Examiner contends that Applicants' arguments are not commensurate in scope with the claimed invention because the claimed invention also includes "modified" sugars (i.e., Applicants use of "comprising" terminology does not preclude this possibility). In addition, Fodor et al refute this argument because they provide an example where enzymatic synthesis was used to synthesize a complex carbohydrate on a chip starting with the "modified" sugars (e.g., see Fodor et al, columns 68-69, Section V B, see especially column 69, paragraph 2). Applicants provide no evidence to support this statement especially with regard to the reaction conditions and enzymes employed in Fodor et al.

[6] Finally, the Examiner further contends that in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (e.g., claims 65 and 68-69 does not mention the use of a linker) are

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not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Accordingly, the 35 U.S.C. § 102(b) rejection cited above is hereby maintained.

### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.  
January 9, 2004

Jon D. Epperson  
